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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/738,742 | 12/15/2000 | Jason Hill | CUB-4 US | 2149 |

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| EXAMINER | |
|---|---|
| LUKTON, DAVID | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/738,742 | HILL ET AL. | |
| | Examiner | Art Unit | |
| | David Lukton | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2,5-12,15-27 and 30-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5-12, 15-27, 30-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the amendment filed 12/8/03, claims 16, 24, 25 have been amended. Claims 1, 2, 5-12, 15-27, 30-36 remain pending. Applicants' arguments filed 12/8/03 have been considered and found not persuasive.

*

Claims 1 and 2 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending application Serial No. 09/739,535. Although the conflicting claims are not identical, they are not patentably distinct from each other. There is overlap of the claimed genera.

[This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The response filed 12/8/03 argues that a response will be provided after the claims are indicated to be allowable. However, in cases where an obviousness double patenting (ODP) rejection is justified, it is appropriate to defer mailing of a Notice of Allowability (at least) until after the ODP rejection has been overcome.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application . See 37 CFR 1.78(d)

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 is rejected under 35 U.S.C. §112, first paragraph, for the reasons set forth in the objection to the specification.

Claim 30 is drawn to a method of converting a compound of claim 27 into a compound of claim 1 or 2. As indicated in the previous Office action, the specification does not explain how to do this. Suppose, for example, that the "target" compound is one falling within the scope of claim 1 wherein "X" (of claim 1) is -S=O or $SO_2$. How would one go about replacing the group -NH-CO-NH- with the group -NH-SO-NH- or with the group -NH-$SO_2$-NH-...? Or suppose that, in claim 1, "B" is allyl, "X" is -C=NH- , and "A" is hydrogen. What process steps would a chemist undertake? It appears that the specification is silent on this matter.

The amendment to claim 30 is noted, but this is not effective to overcome this ground of rejection.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-26 and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 16 recites that bacterial infections can be "controlled" or "eliminated". The second of these terms implies that fully 100% of the bacteria present can be eliminated, and that this will occur in 100% of test subjects. The term "controlled" encompasses both reduction in the amount of bacteria, and its outright elimination. However, enablement is absent for the case of outright elimination of bacterial infections. As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988), the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

It is true that the specification discloses (pp. 63-65) that the lifetimes of infected rats can be extended, wherein the rats are infected with a particular strain of *S. areus*. In accordance therewith, it is stipulated that a claim drawn to a method of treating bacterial infections would be enabled insofar as amelioration or mitigation of the symptoms is

concerned. But outright elimination of all bacterial cells in all subjects is another matter.

First, the term "bacterial infection" would encompass a wide range of diseases, and not limited to just those caused by *S. areus*. For example, the following diseases would be encompassed:

> Anthrax, cholera, conjunctivitis, nosocomial infections, otitis media, pelvic inflammatory disease, plague, pneumonia, dengue fever, elephantiasis, rabies, rheumatic fever, roseola, rubella, syphillis, gonnorhea, clamydia, helicobacter pylori, "mucosa-associated lymphoid tissue" resulting from helicobacter pylori, smallpox, strep throat, septicemia, sickle cell anemia, ulcers, tetanus, toxic shock syndrome, lassa fever, leprosy, lyme disease, typhoid fever, measles, meningitis, trachoma, toxoplasmosis, tuberculosis, whooping cough, yellow fever, diarrhea, brucellosis, diptheria, coccidiodiomycosis, and cold sores.

There is no evidence that any of these diseases can be successfully treated. Thus, even if it were the case that 100% of all *S. areus* bacteria could be eliminated from a host, it would not follow that other bacteria would be effected to the same degree; it is likely that many bacteria will be resistant (to the claimed compounds) altogether. This matter of antibiotic resistance is disclosed in, e.g., the following references:

Liu (*Advances in Experimental Medicine and Biology* 455, 387 1999)

Monroe (*Current Opinion in Microbiology* 3(5) 496-501, 2000).

Specifically with regard to endotoxin-associated conditions, consider the following: Corriveau C. C. "Antiendotoxin therapies for septic shock" (*Infectious Agents and Disease*, **2** (1) 44-52, 1993) discloses that there have been numerous attempts over the years to treat

human septic shock by inhibiting, neutralizing, or clearing endotoxin, and that the results of those attempts support a conclusion of "unpredictability" in the treatment of the same. Death from septicemia is not uncommon, even among patients who are in hospitals and under physician care.

The claims would also encompass treatment of AIDS patients suffering from opportunistic bacterial infections. As is known to the skilled microbiologist, it is not uncommon for an AIDS patient to die from a bacterial infection, despite having been administered a compound which has been used successfully to treat other (otherwise healthy) patients suffering a similar bacterial infection.

As indicated above, the extrapolation undertaken is that from a showing that symptoms of *S. areus* infections can be ameliorated in rats, to an assertion that 100% of all bacterial species can be totally eliminated from 100% of all test subjects. The skilled microbiologist would conclude that such an extrapolation will produce "unpredictable" results. The specification also does not provide evidence from the prior art that there exist compounds which will eliminate 100% of all bacterial species from 100% of all test subjects. The specification provides no guidance as to how to use the claimed compounds to eliminate 100% of all bacterial species from 100% of all test subjects. Accordingly, "undue experimentation" would be required to "control or eliminate" all bacteria from all infected subjects.

*

Claims 1, 2, 5-12, 15-27, 30-36 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 1, the second line of text following the structure (formula (I)), the following is recited: "wherein R is:". On the line of text following this, a formula is recited which contains substituent variables "X" and "A". However, this formula is incomplete in that both "B" and the nitrogen atom (to which "B" is bonded) are missing. In addition to the foregoing, the same error is present in the line following the phrase "wherein $R^1$ is".

- In claim 2, the following is recited: "wherein $R^1$ is:". On the line of text following this, a formula is recited which contains substituent variables X' and A'. This formula is incomplete in that both B' and the nitrogen atom (to which B' is bonded) are missing.

- In claim 7, the structural formula is incomplete.

- In claim 8, oxygen atoms and nitrogen atoms are missing from the structures.

- In claim 9, the first structure (containing $R^{12}$) contains a typographical error.

- In claim 10, it appears that two sulfur atoms are missing from the first structure.

- In claim 11, the first structure contains two errors.

- In claim 23, "SEQ ID NO; 1" should instead be: - - SEQ ID NO: 1 - - .

- There are three typographical errors in claim 27. In the recited structure, the tripeptide Asp-Asn-Trp is intended to be bonded to the amino group of threonine. However, the amide nitrogen atoms are missing from two of the residues (i.e., Asp and Asn). In addition, the indole nitrogen atom is missing from the tryptophan.

- Claim 30 is indefinite as to the process steps. For example, if the compound of claim 1 or 2 were placed in a vial, would the recited conversion take place spontaneously, or are there steps which a chemist would have to undertake?

- In claim 31, nitrogen atoms are missing from subsituents of compound numbers 5 and 71.

- In claim 34, the structural formula is incomplete.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

✺

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at 571-272-0951. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

D. Lukton # 2/17/04

Christopher S. Low

CHRISTOPHER S. F. LOW
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